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CASWELL FILE

Glyphosate / Tox

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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MEMORANDUM:

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: EPA Reg. #: 524-308; Roundup; Glyphosate; Pathology Report on Additional Kidney Sections
Caswell No. 661A
Accession No. 259621

TO: Robert Taylor
Product Manager (25)
Registration Division (TS-767)

THRU: Robert P. Zendzian, Ph.D. 12/12/85
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Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: William Dykstra, Ph.D. William Dykstra 12/12/85
Toxicology Branch
Hazard Evaluation Division (TS-769)

12/12/85

Requested Action:

Review pathology report on additional kidney sections.

Background:

Glyphosate was considered oncogenic in male mice causing renal tubule adenomas, a rare tumor, in a dose-related manner. The incidence of this tumor was 0, 0, 1, and 3 in the control, low-, mid-, and high-dose groups, respectively.

Additional evaluation of all original renal sections identified a small renal tubular adenoma in one control male (animal No. 1028) which was not diagnosed as such in the original pathology report.

Subsequently, Toxicology Branch recommended that additional renal sections be cut and evaluated from all control and glyphosate treated male mice.

This review contains the evaluation of the submitted results of the additional sectioning and pathological data.

Conclusion:

The results of the additional pathological evaluation on re-cut kidney sections in male mice demonstrated no additional tumors were present. The significance of this finding will be determined later by the Ad Hoc committee.

Review:

1. The pathology report of additional kidney sections submitted by the registrant (Monsanto) showed that the renal tubule adenoma incidence in male mice was as follows:

Dose (ppm)	0	1000	5000	30,000
Animal number			3023	4029,4032,4041
Renal tubule adenoma	0	0	1	3
No. examined	49	49	50	50

The additional tumor in the control group which had been diagnosed from the re-evaluation of the original slides was not present in the re-cut kidney sections.

Toxicology Branch's pathologist (report attached) stated that the control tumor "does not represent a pathophyioloically significant change".

Statistical analysis of the tumor results showed no significant ($P<0.05$) difference in the incidence of renal tubule adenoma between control and treated groups.

However, the test for linear trend in proportions resulted in a $p=0.016$ which is statistically significant.

According to the registrant's pathology report, non-neoplastic kidney lesions did not reveal evidence of an ongoing chemically induced neprotoxicity.

Based on the original report and the new report, Toxicology Branch concludes that chronic interstitial nephritis occurred in compound-related manner in males at the high-dose as is shown below:

	Males (Chronic Interstitial Nephritis)			
Dose (ppm)	0	1000	5000	30,000
Incidence				
Original report	5/49	2/49	7/50	12/50
New report	5/49	1/49	7/50	16/50